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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,962	02/25/2000	Thomas C. Terwilliger	S-91,732	7573

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EXAMINER

MARSCHER, ARDIN H

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 05/20/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/512,962	TERWILLIGER, THOMAS C.	
	Examiner	Art Unit	
	Ardin Marschel	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-14 is/are pending in the application.
~~2) ☒ Claim(s) 1-9 have been canceled. ~~3) ☒ Claim(s) 1-9 have been canceled.~~~~
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

Unfortunately, applicant's response, filed 10/19/01, to the previous Office action, mailed 8/21/01, as Paper No. 5, was inadvertently misplaced for several months.

Applicant is hereby informed that examination, however, is hereby continued at this time.

In applicant's amendment, filed 10/19/01, a shift of restriction group was indicated as a divisional case to continue prosecution based on original claims 1-5, rather than original claims 6-9 as elected in Paper No. 4, filed 6/22/01. Although such a shift of invention under examination to a different restriction group is generally not permitted (See the MPEP at section 819.), the election is hereby waived and the shift is hereby permitted in this situation due to the lengthy delay in further examination due to the above inadvertent paper misplacement. (See the MPEP at section 819.01.)

It is noted that claims 1-9 have been canceled and claims 10-14 have been newly submitted in said amendment, filed 10/19/01.

Applicants' arguments, filed 10/19/01, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

NON-STATUTORY SUBJECT MATTER

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10-14 are rejected under 35 U.S.C. § 101 because the claims are directed to non-statutory subject matter.

Consideration of the "Computer-Related Inventions" section 2106 of the MPEP, part B., subpart 2.(b), has revealed that the instant claims are directed to non-statutory subject matter. The instant claims are directed to computational methods for improving an electron density map without requiring the performance of a result outside of a computer or computation device and thus manipulates concepts or converts data, in this case electron density data without resulting in any physical transformation outside of a computer or other computational device. The instantly claimed subject matter therefore is non-statutory subject matter under 35 U.S.C. § 101.

LACK OF ENABLEMENT

Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples,

(4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board of Appeals also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

It is noted that the claims require the practice of forming histograms of electron densities in steps a. and e. of claim 10 and therefore in claims dependent therefrom. Consideration of the instant specification reveals that the only guidance for such histogram forming is set forth in a publication incorporated by reference on page 16, lines 6-10. Since the formation of said histograms are clearly required steps in the claimed method said formation practice is essential subject matter for the practice of the instant claims. No other guidance for this histogram forming has been found as filed. It is noted that the electron densities of proteins is a complex concept with well known complexities of electron orbital theory and/or quantum mechanical representations of electron wave/particle characteristics, thus making it undue experimentation to perform said forming without significantly detailed guidance. It is improper to incorporate by reference the practice of essential subject matter. See the following paragraph regarding this issue.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to

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amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

LACK OF ENABLEMENT

Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board of Appeals also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

It is noted that the claims require the practice of at least 2 equations as set forth in claim 10, steps c. and f. Within these equations are parameters as listed in lines 9-11 and 19-21. The enabling procedures for calculating these parameters has not been found as filed. It is noted that a general description of least-squares fitting is set forth on page 15, lines 22-24, but without any significant details thereof, or in the preceeding paragraphs on pages 13-15 of the instant specification. Such a complex set of 6 parameters regarding fitting to a complex map of electron densities in a protein as required for the practice of the instant claims is deemed undue experimentation without detailed methodology set forth in the instant specification.

LACK OF ENABLEMENT

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue

experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board of Appeals also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

It is noted that claim 14 requires the practice of a Fast Fourier Transform. Consideration of the instant specification reveals that the only guidance for such a Transform is set forth in a publication incorporated by reference on page 10, lines 13-18. Since the this Fast Fourier Transform is clearly a required step for the practice of claim 14, said Transform practice is essential subject matter for the practice of the instant claims. No other guidance for this Transform practice has been found as filed. It is noted that the electron densities of proteins is a complex concept with well known complexities of electron orbital theory and/or quantum mechanical representations of electron wave/particle characteristics, thus making it undue experimentation to perform said Fast Fourier Transform without significantly detailed guidance. It is improper to incorporate by reference the practice of essential subject matter. See the following paragraph regarding this issue.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

LACK OF ENABLEMENT

Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those

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in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board of Appeals also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

It is noted that the claims require the practice of identifying both protein and solvent regions of electron densities in steps b. and e. of claim 10 and therefore in claims dependent therefrom. Consideration of the instant specification reveals that the the guidance for such region defining includes the requirement for estimation of modification of these regions as set forth in a publication incorporated by reference on page 12, lines 8-14. Since the defining of said regions is clearly required steps in the claimed method said defining practice is essential subject matter for the practice of the instant claims. No other guidance for this region defining estimation and modification has been found as filed. It is noted that the electron densities of proteins is a complex concept with well known complexities of electron orbital theory and/or quantum mechanical representations of electron wave/particle characteristics, thus making it undue experimentation to perform said forming without significantly detailed guidance. It is improper to incorporate by reference the practice of essential subject matter. See the following paragraph regarding this issue.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to

amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

SCOPE OF ENABLEMENT

Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling (subject to satisfying the above lack of enablement rejections) for the practice of log-likelihood determination of step g. of claim 10 as set forth in the instant specification on page 12, lines 2-7, it does not reasonably provide enablement for an unspecified generic log-likelihood determination as set forth in said step g. of claim 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples,

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(4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board of Appeals also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

It is noted that the claims require the practice of determination of the log-likelihood of electron densities in step g. of claim 10 and therefore in claims dependent therefrom. Consideration of the instant specification reveals that the only guidance for such a determination is set forth on page 12, lines 2-7, of the instant specification. Since the determination of said log-likelihood is clearly a required step in the claimed method said determination practice is essential subject matter for the practice of the instant claims. No other guidance for this determination has been found as filed. It is noted that the electron densities of proteins is a complex concept with well known complexities of electron orbital theory and/or quantum mechanical representations of electron wave/particle characteristics, thus making it undue experimentation to perform said determination without significantly detailed guidance.

VAGUENESS AND INDEFINITENESS

Claims 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 10, part i., the process of iterating the forming of revised log-likelihood structure factor values is set forth, but without defining the metes and bounds of what revisions would reduce changes to converge to being below a predetermined value. It is confusing that the claims lack any definition of what revision will result in said reduction of changes as needed to produce said changes to be below any particular predetermined value. Clarification via clearer claim wording is requested. This unclarity also exists in claims 11-14 due to their dependence from claim 10.

INFORMALITIES

The disclosure is objected to because of the following informalities:

Internal periods, ".", within claims are only permitted regarding abbreviations. It is noted that claim 10 contains improper periods at each of the part designations, such as, at "a.", "b.", etc. Claims 12-14 also contain corresponding improper internal periods.

In claim 10, part f., the capitalization confusingly is different for the subscript in σ_{MAP} in the equation in part f. vs. in the description in the last 2 lines of said part f., therein given as σ_{map} .

Appropriate correction is required.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is

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(703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

May 16, 2003

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER